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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference LDS-0527	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/14351	International filing date *(day/month/year)* 24 JUNE 1999	Priority date *(day/month/year)* 26 JUNE 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 9/27, 31/56 and US Cl.: 424/450; 514/179, 180		
Applicant LDS TECHNOLOGIES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26 JANUARY 2000	03 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer F.T. MOEZIE Telephone No. (703) 308-0193

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/14351

I. Basis of the report

1. With regard to the **elements** of the international application:*

[ ] the international application as originally filed

[X] the description:
pages 1-24 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

[X] the claims:
pages NONE , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages 25-28/2 , filed with the demand
pages NONE , filed with the letter of

[X] the drawings:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. 2-4

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Inte[redacted]nal application No.
PCT/US99/14351

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1 and 5-33	YES
	Claims	none	NO
Inventive Step (IS)	Claims	1 aqnd 5-23	YES
	Claims	none	NO
Industrial Applicability (IA)	Claims	1 and 5-23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1 and 5-33 lack an inventive step under PCT Article 33(3) as being obvious over LY et al. in view of US patent to Benjamin et al No. 4,782,047.

Benjamin et al teach the use of anti-inflammatory steroids in aqueous formulation for nasal administration. See the entire document. However, the primary reference does not teach the use of high-HLB surfactant component in the composition. The article to Ly et al discloses that tocopherol ester-linked polyethylene glycol succinate 1000 (TPGS) is known to have a high-HLB value and "have potential as enhancers of the aqueous solubility of poorly water soluble drugs". It would have been obvious and expected to an ordinary art skilled at the time the invention was made to use the high-HLB surfactant taught by the secondary reference into the primary reference's composition with the expectation of success-absent evidence of unexpected findings.

Claims 1 and 5-33 meet the criteria set out in PCT Article 33(2) and(4), because the prior art does not teach the compositions as claimed. Moreover the claims find industrial applicability in the field of medicine.

---------- NEW CITATIONS ----------
NONE

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1 and 5-21 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): The terminology "high" is a relative term and reders the claims unclear as to their metes and bounds.

What is claimed is:

1. A composition suitable for administering a therapeutic dose of a corticosteroid to the respiratory tract, consisting essentially of:

(a) from 5 μg/ml to about 5 mg/ml of a corticosteroid in dissolved form;

(b) from about 0.1 to about 20 percent by weight of a pharmaceutically acceptable, high-HLB surfactant component, wherein the HLB of the surfactants present in the high-HLB surfactant component is greater than about 10, and wherein the high-HLB surfactant component comprises at least 50% by weight of an ethoxylated derivative of vitamin E; and

(c) at least about 70 weight percent aqueous phase.

2. Cancel.

3. Cancel.

4. Cancel.

5. The composition of claim 1 wherein the corticosteroid comprises beclomethasone dipropionate.

6. The composition of claim 1 wherein the corticosteroid comprises budesonide.

7. The composition of claim 1 wherein the corticosteroid comprises triamcinolone acetonide.

8. The composition of claim 1 wherein the corticosteroid comprises fluticasone propionate.

9. The composition of claim 1 wherein the corticosteroid comprises flunisolide.

10. The composition of claim 1 wherein the high-HLB surfactant component comprises at least 50% by weight tocopheryl polyethylene glycol 1000 succinate.

11. Cancel.

12. A composition suitable for administering a therapeutic dose of a corticosteroid to the respiratory tract, comprising:

(a) from 5 μg/ml to about 5 mg/ml of a corticosteroid in dissolved form;

(b) from about 0.1 to about 20 percent by weight of a high-HLB surfactant component wherein the HLB of the surfactants present in the high-HLB surfactant component is greater than about 10, and wherein the high-HLB surfactant component comprises at least 50 percent by weight of an ethoxylated derivative of vitamin E; and

(c) at least about 70 weight percent aqueous phase.

13. The composition of claim 12 wherein the high-HLB surfactant component comprises at least 75 percent by weight of an ethoxylated derivative of vitamin E.

14. The composition of claim 12 wherein the high-HLB surfactant component comprises at least 90 percent by weight of an ethoxylated derivative of vitamin E.

15. The composition of claim 12 further comprising from about 0.1 to about 20 percent by weight of a pharmaceutically acceptable cosolvent comprising propylene glycol, polyethylene glycol having a molecular weight between about 200 and 4000, glycerol, ethoxydiglycol, glycofurol, and ethanol, or a combination thereof.

16. The composition of claim 12 further comprising from about 0.1 to about 3 percent by weight of a low HLB surfactant having an HLB below about 8.

17. The composition of claim 12 further comprising from about 0.1 to about 3 percent by weight of an oil.

18. A method for administering a therapeutic dosage of a corticosteroid to the respiratory tract, comprising:

(a) providing a corticosteroid composition comprising:

(1) from 5 μg/ml to about 5 mg/ml of a corticosteroid in dissolved form;

(2) from about 0.1 to about 20 percent by weight of a high-HLB surfactant component wherein the HLB of the surfactants present in the high-HLB surfactant component is greater than about 10, and wherein the high-HLB surfactant component comprises at least 50 percent by weight of an ethoxylated derivative of vitamin E; and

(3) at least about 70 weight percent aqueous phase;

(b) aerosolizing the corticosteroid composition; and

(c) administering a therapeutic effective dosage of the aerosol of the corticosteroid composition by inhalation.

19. The method of claim 18 wherein the corticosteroid composition consists essentially of said corticosteroid, said aqueous phase, and said high-HLB surfactant.

20. A method for administering a therapeutic dosage of a corticosteroid to the nasal passage, comprising:

(a) providing a corticosteroid composition comprising:

(1) from about 50 μg/ml to about 10 mg/ml of a corticosteroid in dissolved form;

(2) from about 0.1 to about 20 percent by weight of a high-HLB surfactant component wherein the HLB of the surfactants present in the high-HLB surfactant component is greater than about 10, and wherein the high-HLB surfactant component comprises at least 50 percent by weight of an ethoxylated derivative of vitamin E; and

(3) at least about 70 weight percent aqueous phase;

(b) administering a therapeutic effective dosage of the corticosteroid composition by nasal inhalation.

21. A method of preparing a diluted corticosteroid composition containing the corticosteroid in a dissolved form, comprising:

(a) dissolving a corticosteroid compound into a molten pharmaceutically acceptable high-HLB surfactant component, wherein the HLB of the surfactants present in the high-HLB surfactant component is greater than about 10, and wherein the high-HLB surfactant component comprises at least 50 percent by weight of an ethoxylated derivative of vitamin E;

(b) subsequently blending the molten high-HLB surfactant component containing the dissolved corticosteroid with an aqueous phase,

wherein the aqueous phase is present in an amount of at least about 70 weight percent, and the high-HLB surfactant component is present in an amount of from about 0.1 to about 20 weight percent of the diluted corticosteroid composition.

22. The composition of claim 1 wherein the ethoxylated derivative of vitamin E comprises at least 75% by weight of the high-HLB surfactant component.

23. The composition of claim 1 wherein the ethoxylated derivative of vitamin E comprises at least 90% by weight of the high-HLB surfactant component.

24. The composition of claim 1 wherein the high-HLB surfactant component comprises at least 75% by weight tocopheryl polyethylene glycol 1000 succinate.

25. The composition of claim 1 wherein the high-HLB surfactant component comprises at least 90% by weight tocopheryl polyethylene glycol 1000 succinate.

26. The composition of claim 12 wherein the high-HLB surfactant component comprises at least 75% by weight tocopheryl polyethylene glycol 1000 succinate.

27. The composition of claim 12 wherein the high-HLB surfactant component comprises at least 90% by weight tocopheryl polyethylene glycol 1000 succinate.

28. The method of claim 18 wherein the ethoxylated derivative of vitamin E comprises at least 75% by weight of the high-HLB surfactant component.

29. The method of claim 18 wherein the high-HLB surfactant component comprises at least 75% by weight tocopheryl polyethylene glycol 1000 succinate.

30. The method of claim 20 wherein the ethoxylated derivative of vitamin E comprises at least 75% by weight of the high-HLB surfactant component.

31. The method of claim 20 wherein the high-HLB surfactant component comprises at least 75% by weight tocopheryl polyethylene glycol 1000 succinate.

32. The method of claim 21 wherein the ethoxylated derivative of vitamin E comprises at least 75% by weight of the high-HLB surfactant component.

33. The method of claim 21 wherein the high-HLB surfactant component comprises at least 75% by weight tocopheryl polyethylene glycol 1000 succinate.